

as to offer consistent capsule disintegration during dissolution process. A capsule-filling machine should possess certain features for successful use during manufacturing. These features include

- Ability to maintain the product in the molten state before dosing
- Accurate dosing of liquid volumes ranging from 0.1 to 1.0 mL
- Surveillance systems to halt dosing when the absence of a capsule body in the die is detected

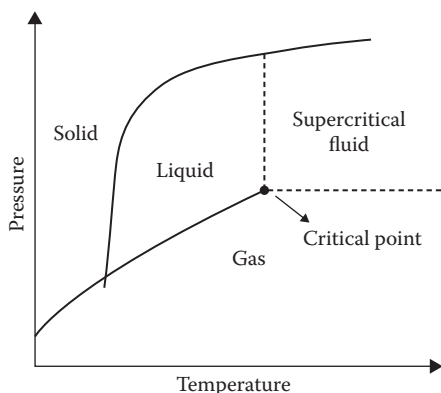
A successful scale-up of capsule-filling process was demonstrated, for instance, in one study, using a Qualifill semiautomated or H&H capsule filler (Robinson 2001). Gelucire 50/12 or Precirol (a wax comprised of mono-, di-, and triglycerides of palmitostearic acid) was filled into size 2 capsules at a fill weight of 269 mg and at a filling temperature between 50°C and 52°C. Qualifill capsule filler yielded capsules with highly uniform fill weights of less than 1% relative standard deviation.

### SPRAY DRYING

Spray drying is a process where a solution of drug substance and carrier is evaporated by spraying the solution as fine droplets into a chamber that is maintained under controlled conditions of heat, humidity, and airflow. The dissolution rate of many poorly water-soluble drugs has been enhanced using spray drying (Sethia and Squillante 2003; Ambike et al. 2005). Organic solvents are normally used during spray-drying process as they are easy to evaporate and possess good solvent capacity for many poorly water-soluble drugs. The morphology form of solid dispersion, and consequently the drug dissolution and stability, can be impacted by the process parameters and geometry of equipment. For instance, the particle size of spray-dried solid dispersion can be controlled by varying the concentration of solute in spray-drying liquid and the droplet size during the spray-drying process (Elversson 2003).

### SUPERCRITICAL FLUID TECHNOLOGY

Supercritical fluid (SCF) technology has been successfully applied in particle design engineering of pharmaceuticals, polymer/biomaterials, and chemical compounds (Jung and Perrut 2001). A SCF is a substance that exists above its critical point, which is defined by the conditions of temperature and pressure at which liquid and gaseous states of a substance coexist. When a liquid is heated, its density continues to decrease, while the density of vapor being formed continues to increase. At the critical point, densities of liquid and gas are equal and there is no phase boundary, as shown in Figure 18.6. Above the critical point, that is, in the supercritical region, the fluid possesses the penetrating power typical of a gas and the solvent power typical of a liquid.



**FIGURE 18.6** Supercritical region of a hypothetical compound. The solid lines represent phase boundaries between solid–liquid, liquid–gas, and solid–gas phases. Supercritical region is the region indicated by the dotted line.